see remarks #3

A Mutation in H-Ferritin mRNA, *by Kato et al.*
(p. 191)

Kato et al. have identified a woman who has high serum ferritin levels, increased serum iron and transferrin saturation, and iron deposition in hepatocytes, Kupffer cells, and macrophages. Three family members also exhibited elevated serum ferritin levels, suggesting a genetic disorder. The prevalent *HFE-1* and *TFR2* mutations that are normally associated with hemochromatosis were not present in this family. However, there was a heterozygous A49T mutation in the 5_UTR of the H-subunit of ferritin. This mutation falls in the iron-responsive element (IRE) of this gene, which is involved in translational control of gene expression. The mutation strengthens the interaction between the IRE and a translational repressor, thereby increasing this repression. Immunoblotting of a liver-biopsy sample from one of the affected individuals confirms the decreased expression of the H-subunit of ferritin, as well as an increase in the L-subunit levels. Cells transfected with a construct encoding the mutated H-subunit show increased uptake of iron but decreased incorporation of ^{59}Fe into ferritin. The authors believe that this results from reductions in the ferroxidase activity of the H-subunit, which are due to decreased production of the protein, because this activity is essential for the incorporation of iron into ferritin. These defects probably lead to the tissue iron deposition seen in the affected individuals.

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Am J. Hum Genet 69: 191-197 (2001)